# Interpretability in atopic dermatitis

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However, the authors used a strict definition for the 'validated algorithm-based' diagnosis of HS, and the sociodemographic characteristics and comorbidities of the 'validated algorithm-based' HS population were consistent with previous studies, minimizing classification bias.

Finally, the authors should be congratulated for the robustness of their study in terms of its design, opening a new methodological avenue in the pharmacoepidemiology field, where diagnostic criteria are lacking. This study confirmed that the prevalence of HS is not more than 0·7–1%.

## Conflicts of interest

None to declare.

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## Interpretability in atopic dermatitis: all about the anchor

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**Linked Article:** Vakharia *et al. Br J Dermatol* 2018; **178**: 925–930.

Proper measurement of the characteristics of a disease is an important topic in medical science. Measurements can be performed to assess characteristics such as severity, symptoms, extent or impairment. They can also be clustered in a construct like health-related quality of life, often covering impairment in several domains (e.g. symptoms, emotions or functioning). Once it is clear how to measure a certain characteristic and which instrument is best suited for this, the next step is to determine how to interpret the outcome of such an instrument.

In this issue of the *British Journal of Dermatology* Vakharia *et al.* present the results of an interpretability study, designed to determine severity strata for several patient-reported outcome (PRO) measurement instruments used in atopic dermatitis (AD): the Patient Oriented Eczema Measure (POEM), Numerical Rating Scale (NRS)-itch, raw/mean ItchyQoL, 5-D itch and Dermatology Life Quality Index (DLQI).[1] When determining strata, measured scores are compared with scores obtained with a single question with clearly labelled answer categories (the 'anchor'), chosen to represent the desired characteristic for interpretation; in this case disease severity.[2]

A difficult issue is that a 'true' disease severity of AD in general does not exist. For example, it matters whether one asks a patient or a physician to judge the disease severity. How should it be judged? Should disease severity incorporate only clinical signs or also symptoms, e.g. itch and pain? Should one ask about the frequency or the intensity of these symptoms? Or should one focus on how much they *bother* a patient?[3,4]

The authors chose to use one broad anchor question for all mentioned instruments: 'Would you describe your atopic dermatitis or eczema as mild, moderate, or severe?' In their validation paper of this single question, the authors conclude that it might be an important PRO for assessing the overall burden of disease that accounts for severity, extent, symptom burden and quality of life impact.[5]

In the current study, the use of this anchor assessing 'overall burden' is probably the main reason why correlations with severity strata of the studied measurement instruments were found to be modest at best (kappa ranging from 0·331 to 0·499). For example, a patient indicating an overall severe burden of AD does not necessarily have to experience severe itching (resulting in a low score for the itch-related instruments). Another explanation could be the lack of a specified time frame for the anchor, while the studied

instruments have time frames of between 7 and 14 days. The authors justly conclude that each of the studied instruments assesses different aspects of the multidimensional impact that AD has on patients, with only partial overlap. This means that each instrument has a potential added value, and measurements with more than one instrument are necessary. Considering this, in future interpretability studies it would be interesting to see the use of anchor questions specifically tailored to the dimension/domain of the studied instrument; for example, anchor questions for the ItchyQoL and 5-D itch should ask about the bother patients experience because of their itch.

An interesting finding is that the strata for NRS-itch had a stronger correlation with the anchor than strata of the POEM. Although POEM was chosen by the Harmonizing Outcome Measurements in Eczema (HOME) group as the preferred core instrument to assess patient-reported symptoms,[6] Vakharia *et al.* suggest considering NRS-itch as an additional assessment.

In conclusion, when interpreting scores from patients, regardless of the disease, one should always be aware of how strata for interpretability were determined. The choice of anchor is often vital for interpretability.

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## Conflicts of interest

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## Supporting Information

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**Audio S1** Author audio.

# Association of *APOE* polymorphisms with multibacillary leprosy

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**Linked Article:** Wang *et al. Br J Dermatol* 2018; **178**:931–939.

In an article in this issue of the *British Journal of Dermatology*, using integrated expression quantitative trait loci, mRNA expression and protein interaction analysis, Wang *et al.*[1] report on some potential genetic associations between the human apolipoprotein E (ApoE) gene and leprosy in Han Chinese patients from Southwest China.

Despite new information mainly at the molecular level, the pathogenesis of leprosy remains poorly understood. Epidemiological studies have shown the importance of host genetic factors in susceptibility to the development of leprosy and the clinical form of the disease. Several chromosomal regions associated with leprosy have been identified in genome-wide linkage analysis.[2]

The *APOE* gene is located in chromosome 19q13 and encodes a member of the family of soluble apolipoproteins with polymorphic alleles carrying homozygous and heterozygous genotypes. The molecular basis of *APOE* single-nucleotide polymorphisms (SNPs) is cysteine–arginine interchanges.[3]

*APOE* SNPs are the main genetic determinant of Alzheimer disease (AD) risk: individuals carrying the ε4 allele are at increased risk of AD compared with those carrying the more common ε3 allele, whereas the ε2 allele decreases the risk.[3] Conversely, in patients with leprosy without dementia, the frequency of the ε4 allele was significantly higher, suggesting that this allele is not a risk factor for dementia in elderly patients with leprosy.[4] Furthermore, histological analyses of brain tissue of elderly patients with leprosy without dementia showed a significantly lower frequency of deposition of β-amyloid, the cue molecule involved in AD, than age-matched controls without dementia.[5] The results suggest that patients with leprosy might have a low risk of AD.

Although the finding is controversial,[6] antileprosy drugs appear to reduce dementia, as shown in elderly patients with leprosy treated with dapsone.[7] Furthermore, rifampicin inhibited the initial step of β-amyloid formation, showing activity against the accumulation and toxicity of intracellular β-amyloid.[8]

Lepromatous leprosy (LL) exhibits extensive involvement of the skin and peripheral nerves. A typical feature of LL is the survival and replication of *Mycobacterium leprae* stored within the